AMENDMENTS TO THE SPECIFICATION

On page 2, at the paragraph beginning on line 14, please amend as follows:

The present inventors have identified Rv3879c as a major T-cell antigen in humans, with 45% of tuberculosis patients responding to peptides from the Rv3879 gene product. Only one of 38 (2.6%) BCG-vaccinated donors responded to peptides from Rv3879c. The ~~highly~~ high specificity of Rv3879c peptides, together with their moderate sensitivity in tuberculosis patients, identify these peptides as candidates for inclusion in new T cell-based tests for MTB infection.

On page 3, at the paragraph beginning at line 32, please amend as follows:

Figure 3 illustrates the location and homology of PPE protein family motif as described (~~http://genolist.pasteur.fr/TubercuLIST/mast/P210.1.html~~ see the TubercuList World-Wide Web Server at the website for the Institut Pasteur), within the partial amino acid sequence of Rv3873 (amino acid residues 100-160) (SEQ ID NO:32 compared to SEQ ID NO:33). Amino acid residues are shown in the one letter code. Underlined residues indicate the given peptide sequence. Identical residues are indicated with a cross.

On page 13, at the paragraph beginning at line 5, please amend as follows:

The peptide is typically made from a longer polypeptide e.g. a fusion protein, which polypeptide typically comprises the sequence of the peptide. The peptide may be derived from the polypeptide by for example hydrolysing the polypeptide, such as using a protease; or by physically breaking the polypeptide. The polypeptide ~~is~~ typically has the sequence shown in SEQ ID NO:1 and may have been expressed recombinantly.

On page 14, at the paragraph beginning at line 7, please amend as follows:

All participants were recruited prospectively in London and Oxford over a 14 month period from June 2002 through July 2003. Ethical approval for the study was granted by the Harrow and Central Oxford Research Ethics Committees. The diagnoses of all 49 TB patients were bacteriologically confirmed with positive cultures for MTB from one or more clinical specimens. Patients were untreated or had received less than 2 weeks therapy at the time of

~~venepuncture~~ venipuncture for ELISPOT assay. Control participants were healthy BCG-vaccinated laboratory personnel from regions with a low prevalence of TB and with no known exposure to MTB. All had recently tested negative by IFN-γ-ELISPOT using 38 overlapping 15-mer peptides spanning the length of ESAT-6 and CFP10, as previously described (Lalvani *et al.* 1997. J. Exp. Med. 186:859-865).

On page 15, at the paragraph beginning on line 19, please amend as follows:

The DNA sequence of MTB H37Rv was visualized using the TubercuList database ~~(http://genolist.pasteur.fr/TubercuList/)~~ (see the world wide website of the Institut Pasteur) Basic Local Alignment Search Tool (BLAST) searches for protein sequence homology in available mycobacterial genomes were performed using TubercuList, the Sanger Centre server (Cambridge, UK) for the incomplete *M. bovis BCG* genome sequence ~~(http://www.sanger.ac.uk/Projects/M_bovis/)~~ (see the world wide website of the Sanger Centre) and the National Center for Biotechnology Information (NCBI) BLAST server ~~(http://www.ncbi.nlm.nih.gov/BLAST)~~ (see the world wide website of the NCBI).

On page 16, at the paragraph beginning at line 7, please amend as follows:

IFN-γ ELISPOT responses of PBMC from all 49 TB patients to the 11 peptide pools from the four antigens are summarized in Fig 1A. The percentages of responding patients varied between 25.5% and 53.1% for the different antigens (Fig 1B). The proportion of patients responding to peptides from each of the antigens Rv3873, Rv3879c, Rv3878 and Rv1989c was 53.1% (95% CI 39-67%), 44.7% (95% CI 31-57%), 34.7% (95% CI 22-48%) and 25.5% (95% CI 13-39%), respectively (Fig. 1B). Combining these responses, 30 of 49 tuberculosis patients responded to peptide pools from one or more antigens, giving a diagnostic sensitivity of 61.2% (95% confidence interval [CI] 46.2%-74.8%) for all peptides used together. This contrasts with the results obtained by Cockle *et al.* 2002 Infect. Immunol. 70:6996-7003 ~~Cockle *et al*~~, who found that peptides from Rv3873, Rv3878, Rv3879c, Rv1989c could together be used to detect almost all infected cattle.

On page 17, at the paragraph beginning at line 4, please amend as follows:

Rv3873 peptide pools elicited responses in 3/38 (7.9%) BCG-vaccinated unexposed donors; Rv3878 and Rv3879c each elicited a response in one (2.6%) donor; and Rv1989c elicited no responses. Two donors, donors 20 and 31, each responded to a different peptide from pool 2 of Rv3873, and one, donor 25, responded to pools from the Rv3873, Rv3878 and Rv3879c (Table 2 and Fig 1). Donors 20 and 31 responded to peptides 119-133 (LTATNFFGINTIPIA; SEQ ID No 21) and 139-153 (YFIRMWNQAALAMEV; SEQ ID No 22), respectively, both from pool 2 of Rv3873. Donor 25 responded to peptide 174-188 (LDPGASQSTTNPIFG; SEQ ID No 23) from Rv3873, peptides 16-30 (AAKLAGLVFPQPPAP; SEQ ID No 24) and 61-75 (ESLVSDGLPGVKAAL; SEQ ID No 25) from Rv3878 and 26-40 (DTFYDRAQEYSQVLQ; SEQ ID No 7) from Rv3879c. Combining all these responses, 3 of 38 (7.9%) BCG vaccinated healthy donors responded to one or more antigens, while 81.6% responded to PPD.

On page 17, at the paragraph beginning at line 21, please amend as follows:

BLAST searches for protein sequences highly homologous to the six 15mer peptides that gave a response in BCG-vaccinated donors were performed. Peptide 119-133 (LTATNFFGINTIPIA; SEQ ID No 21), had the greatest homology with 93% identity to other mycobacterial proteins (14 out of 15 amino acids identical). This peptide is from pool 2 of Rv3873, a member of the PPE family of proteins, and is encoded within a 52 a.a. long motif that is highly conserved throughout the PPE family (Fig. 3). Consequently it displays high levels of homology with many MTB, *M. bovis* and *M. leprae* PPE proteins (Table 3) that are encoded in the deleted and undeleted regions of the genomes of MTB, *M. bovis* and other mycobacteria. Peptide 139-153 (YFIRMWNQAALAMEV; SEQ ID No 22), which is also encoded within the 52 a.a. conserved motif of Rv3873 (Fig. 3), also showed homology with sequences from many PPE proteins (Table 3) although the level of identity was considerably lower at 47% (7 out of 15 identical residues). In contrast, peptide 174-188 (LDPGASQSTTNPIFG; SEQ ID No 23) from Rv3873, which lies outside the conserved motif region, had no significant homology with PPE family members. The two cross-reactive peptides from Rv3878 and the single cross-reactive peptide from Rv3879c, had no significant sequence homology with any other mycobacterial proteins.

On page 18, at the paragraph beginning at line 20, please amend as follows:

CMI to the antigens in this study has previously been assessed in cattle (Cockle *et al.* 2002 Infect. Immunol.. 70:6996-7003). Despite being encoded in RD1, peptides derived from Rv3873 and Rv3879c elicited IFN-γ responses in a whole blood ELISA assay in 17% and 33% of BCG-vaccinated cattle respectively. However, the responses were only borderline positive, and the number of vaccinated cattle tested was low (n=6). In our larger series of BCG-vaccinated humans, we have shown that the level of cross-reactivity of these antigens with BCG is far lower than in cattle. Moreover, 3 of the 5 responses observed were borderline positive (Fig. 2B).

On page 22, beginning at line 4, please amend as follows:

Designation[a]	**Putative Function**	**Amino Acid Sequence**[b]
Rv3873	***M. tuberculosis* PPE family**	**LTATNFFGINTIPIA;** SEQ ID No 21
Rv3021c,3018c,0280,1387	*M. tuberculosis* PPE family	LVATNFFGINTIPIA; SEQ ID No 26
Rv0256c	*M. tuberculosis* PPE family	LMATNFFGINTIPIA; SEQ ID No 27
Rv0453	*M. tuberculosis* PPE family	MVATNFFGINTIPIA; SEQ ID No 28

(ii) Peptide 139-153

Designation[a]	**Putative Function**	**Amino Acid Sequence**[b]
Rv3873	***M. tuberculosis* PPE family**	**YFIRMWNQAALAMEV**; SEQ ID No 22
Rv2768c,1039c	*M. tuberculosis* PPE family	HYGEMWAQDALAMYG; SEQ ID No 29

Rv0286 *M. tuberculosis* PPE family DYVRMWLQAAAVMGL; SEQ ID No 30

Rv1807 *M. tuberculosis* PPE family QYAEMWSQDAMAMYG; SEQ ID No 31

The homology search was performed using the BLAST program.

[a]Designation of *M. tuberculosis* proteins as described~~(18)~~. Sequences of all related proteins described are also present in the *M. bovis* BCG genome ~~(http://www.sanger.ac.uk/Projects/M_bovis/)~~ (see the world wide website of the Sanger Centre). Non-identical residues are underlined.

[b]Amino acid residues are shown in the one letter code.

On page 22, at the paragraph beginning at line 22, please amend as follows:

929 child (<16 yrs) household contacts of sputum smear positive pulmonary TB patients in Istanbul, Turkey (TB prevalence of 41/100, 000) were recruited. All children underwent a Mantoux test, clinical assessment, chest x-ray and had a 10 ml blood sample taken for RD1 and RD2 based IFN-γELISPOT assay using purified, whole recombinant antigen from ESAT-6 and CFP10; and peptides (15mers overlapping by 10) from ESAT-6, CFP10, Rv3873, Rv3878, Rv3879c and Rv1989c (see Table 2 for the exact region of the molecule which was represented in the IFN- γ ELISPOT assay~~.~~). Demographic data was also collected including age, sex and BCG status~~.~~ ~~With~~ with peptide-pools derived from Rv3873, Rv3878, Rv3879c and Rv1989c.

On page 25 on the third line, please amend as follows:

ESAT6/CFP10 (~~ags/peps~~ antigens/peptides)	46.6

Pools	53.2
Pools excluding Pool 2 of Rv3873	43.1
Pools excluding Pool 2 of Rv3873 and Pools 1 to 3 of 1989c	31.9
ESAT 6/CFP10 (ags/peps) and Pools excluding Pool 2 of Rv 3873	62.8

On page 29, at line 1, please amend as follows:

ESAT-6; SEQ ID No 19

MTEQQWNFAGIEAAASAIQGNVTSIHSLLDEGKQSLTKLAAAWGGSGSEAYQ GVQQKWDA TATELNNALQNLARTISEAGQAMASTEGNVTGMFA

CFP10; SEQ ID No 20

MAEMKTDAATLAQEAGNFERISGDLKTQIDQVESTAGSLQGQWRGAAGTAA QAAVVRFQE AANKQKQELDEISTNIRQAGVQYSRADEEQQQALSSQMGF